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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  DEC 01  ChemPort single article sales feature unavailable
 NEWS  3  JUN 01  CAS REGISTRY Source of Registration (SR) searching
                  enhanced on STN
 NEWS  4  JUN 26  NUTRACEUT and PHARMAML no longer updated
 NEWS  5  JUN 29  IMSCOPROFILE now reloaded monthly
 NEWS  6  JUN 29  EPFULL adds Simultaneous Left and Right Truncation
                  (SLART) to AB, MCLM, and TI fields
 NEWS  7  JUL 09  PATDPAFULL adds Simultaneous Left and Right
                  Truncation (SLART) to AB, CLM, MCLM, and TI fields
 NEWS  8  JUL 14  USGENE enhances coverage of patent sequence location
                  (PSL) data
 NEWS  9  JUL 27  CA/CAplus enhanced with new citing references
 NEWS 10  JUL 16  GBFULL adds patent backfile data to 1855
 NEWS 11  JUL 21  USGENE adds bibliographic and sequence information
 NEWS 12  JUL 28  EPFULL adds first-page images and applicant-cited
                  references
 NEWS 13  JUL 28  INPADOCDB and INPAFAMDB add Russian legal status data
 NEWS 14  AUG 10  Time limit for inactive STN sessions doubles to 40
                  minutes
 NEWS 15  AUG 18  COMPENDEX indexing changed for the Corporate Source
                  (CS) field
 NEWS 16  AUG 24  ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
 NEWS 17  AUG 24  CA/CAplus enhanced with legal status information for
                  U.S. patents
 NEWS 18  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS 19  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 14:06:01 ON 29 SEP 2009

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DICTIONARY FILE UPDATES:  27 SEP 2009  HIGHEST RN 1186379-81-6

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=>
Uploading C:\Program Files\Stnexp\Queries\10574489.str
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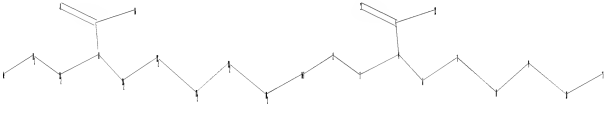

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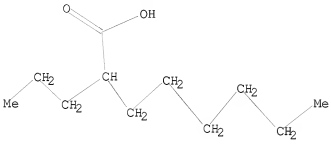
chain nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13
chain bonds :
1-2  2-3  3-4  4-5  4-6  5-12  5-13  6-7  7-8  8-9  9-10  10-11
exact bonds :
1-2  2-3  3-4  4-5  4-6  6-7  7-8  8-9  9-10  10-11
normalized bonds :
5-12  5-13


Match level :
1:CLASS  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  12:CLASS  13:CLASS
```

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



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=> s l1 full
FULL SEARCH INITIATED 14:06:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 594546 TO ITERATE

100.0% PROCESSED 594546 ITERATIONS 38 ANSWERS
SEARCH TIME: 00.00.06

L2 38 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	185.88	186.10

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FILE COVERS 1907 - 29 Sep 2009 VOL 151 ISS 14
FILE LAST UPDATED: 28 Sep 2009 (20090928/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

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The ALL, BIB, MAX, and STD display formats in the CA/CAplus family
of databases have been updated to include new citing references
information. This enhancement may impact record import into
database management software. For additional information, refer
to NEWS 9.

```
=> s l2
L3          80 L2

=> s l3 and (infarction or cerebral or stroke or neural or regeneration or
neurodegeneration)
         50883 INFARCTION
        119523 CEREBRAL
         44645 STROKE
         95204 NEURAL
        133849 REGENERATION
         12874 NEURODEGENERATION
L4          34 L3 AND (INFARCTION OR CEREBRAL OR STROKE OR NEURAL OR REGENERATI
               ON OR NEURODEGENERATION)

=> d ibib i-
'I-' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
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SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations
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HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
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L4   ANSWER 1 OF 34  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2009:68314  CAPLUS
DOCUMENT NUMBER:          150:463976
TITLE:                    Methodological Quality of Animal Studies of
                          Neuroprotective Agents Currently in Phase II/III Acute
                          Ischemic Stroke Trials
AUTHOR(S):                Philip, Maria; Benatar, Michael; Fisher, Marc; Savitz,
                          Sean I.
CORPORATE SOURCE:         Department of Neurology, Houston Medical School,
                          University of Texas, Houston, TX, 77030, USA
SOURCE:                   Stroke (2009), 40(2), 577-581
                          CODEN: SJCCA7; ISSN: 0039-2499
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          65    THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d ibib hit 1

L4   ANSWER 1 OF 34  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2009:68314  CAPLUS
DOCUMENT NUMBER:          150:463976
TITLE:                    Methodological Quality of Animal Studies of
                          Neuroprotective Agents Currently in Phase II/III Acute
                          Ischemic Stroke Trials
AUTHOR(S):                Philip, Maria; Benatar, Michael; Fisher, Marc; Savitz,
                          Sean I.
CORPORATE SOURCE:         Department of Neurology, Houston Medical School,
                          University of Texas, Houston, TX, 77030, USA
SOURCE:                   Stroke (2009), 40(2), 577-581
                          CODEN: SJCCA7; ISSN: 0039-2499
PUBLISHER:                Lippincott Williams & Wilkins
```

DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Methodological Quality of Animal Studies of Neuroprotective Agents Currently in Phase II/III Acute Ischemic Stroke Trials

AB Background and Purpose: Numerous neuroprotective agents have proven effective in animal stroke studies, but every drug has failed to achieve its primary outcome when brought forward to clin. trials. We analyzed the quality and adequacy of animal studies supporting the efficacy of NXY-059 and other neuroprotective agents that are currently being investigated in phase II/III trials. Methods: We conducted a systematic search of all neuroprotective drugs in Phase II or III trials and collected data from animal studies of focal cerebral ischemia testing agents systemically administered within 24 h of occlusion. The methodol. rigor of each individual study was evaluated using 5 criteria derived from the STAIR guidelines. The adequacy of the preclin. "package" for each drug was then evaluated by combining the results of all studies for each drug to determine which of a further 5 STAIR criteria were met before moving forward from animal to human studies. Results: Our search yielded 13 agents of which 10 had published data in peer-reviewed journals. There is substantial within-drug variability in the quality of preclin. studies as well as substantial variation in the completeness of the collective preclin. literature for different drugs. There has been little or no improvement in the quality of animal studies since NXY-059, and current agents have not been subjected to a more complete preclin. evaluation. Conclusion: There is significant heterogeneity in the quality of animal testing for neuroprotective agents in stroke. Drugs in the post-SAINT era have not been subjected to more thorough preclin. evaluation.

ST neuroprotectant NXY 059 cerebral ischemia stroke
erythropoietin caffeinol minocycline

IT Brain ischemia
Human
Neuroprotective agents
Stroke
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of NXY-059 and other neuroprotectants showed heterogeneity in patient with acute ischemic stroke)

IT Albumins, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of albumin showed heterogeneity in patient with acute ischemic stroke)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β; methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of interferon-β showed heterogeneity in patient with acute ischemic stroke)

IT 168021-79-2, NXY-059
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of NXY-059 and other neuroprotectants showed heterogeneity in patient with acute ischemic stroke)

IT 185517-21-9, ONO2506
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of ONO2506 showed heterogeneity in patient with acute ischemic stroke)

IT 823805-47-6, Caffeinol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of caffeinol showed heterogeneity in patient with acute ischemic stroke)

IT 11096-26-7, Erythropoietin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of erythropoietin showed heterogeneity in patient with acute ischemic stroke)

IT 143011-72-7, Granulocyte colony-stimulating factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of granulocyte colony-stimulating factor showed heterogeneity in patient with acute ischemic stroke)

IT 7439-95-4, Magnesium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of magnesium showed heterogeneity in patient with acute ischemic stroke)

IT 10118-90-8, Minocycline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of minocycline showed heterogeneity in patient with acute ischemic stroke)

IT 134234-12-1, Traxoprodil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methodol. quality and adequacy of animal testing for focal cerebral ischemia supporting efficacy of traxoprodil showed heterogeneity in patient with acute ischemic stroke)

=> d ibib hit 2-34

L4 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:721678 CAPLUS
DOCUMENT NUMBER: 149:417318
TITLE: Prophylactic effects of arundic acid (ONO-2506) in the progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice
AUTHOR(S): Kondo, Yogo; Washizu, Makoto; Orima, Hiromitsu; Mori, Takashi
CORPORATE SOURCE: Veterinary Radiology, Nippon Veterinary and Life Science University, Musashino-shi, Tokyo, 180-8602, Japan
SOURCE: Nippon Jui Seimei Kagaku Daigaku Kenkyu Hokoku (2007), 56, 42-51
CODEN: NJSKAM
PUBLISHER: Nippon Jui Seimei Kagaku Daigaku
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: Japanese

TI Prophylactic effects of arundic acid (ONO-2506) in the progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice

AB Recently, it has been shown that the infarct volume increases for the next several days after the induction of ischemia ("delayed infarct expansion"). Yet, it is reported that the occurrence of this phenomenon is closely associated with astrocytic activation in the peri-infarct area, which causes overexpression of S100 protein. Here, we examined the preventive effects on the progression of delayed infarct expansion in the permanent middle cerebral artery occlusion (pMCAO) mouse model using arundic acid (ONO-2506, Ono pharmaceutical co., Ltd.), which is known to oppose astrocytic activation through its inhibitory action on S100B synthesis. The activation of astrocytes in the peri-infarct area was inhibited by the administration of arundic acid, resulting in the significant reduction of GAFP burden (astrocytosis burden)/S100 burden as well as Iba-1 burden (microgliosis burden) in the peri-infarct area. In parallel with the above evidence, the number of TUNEL pos. cells was decreased in the peri-infarct area and delayed infarct expansion was also completely mitigated by the administration of arundic acid. Moreover, the administration of arundic acid significantly improved the exacerbation of neurol. score from 1 day after pMCAO and the effect was showed in every time-point examined Together, the above data showed that the modulation of astrocytic activation though inhibition of S100 protein resulted in the amelioration of delayed infarct expansion as well as the improvement of neurol. deficits after ischemia. Thus, pharmacol. modulation of astrocytic activation by arundic acid may confer a useful therapeutic strategy against acute as well as sub acute ischemic brain damage.

ST prophylaxis arundate ONO2506 neuroprotectant brain ischemia neuron infarction

IT S-100 proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-100B; prophylactic effects of arundic acid (ONO-2506) in progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice)

IT Astrocyte
(activated; prophylactic effects of arundic acid (ONO-2506) in progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice)

IT Brain infarction
Brain ischemia
Neuroprotective agents
Prophylaxis
(prophylactic effects of arundic acid (ONO-2506) in progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice)

IT 185517-21-9, ONO-2506
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prophylactic effects of arundic acid (ONO-2506) in progression of delayed infarct expansion after permanent middle cerebral artery occlusion in mice)

L4 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2007:1300952 CAPLUS
DOCUMENT NUMBER:	147:515078
TITLE:	Histone deacetylase inhibitors for the treatment of neurodegeneration
INVENTOR(S):	Steinkuhler, Christian; Bain, Gretchen; Trauger, John
PATENT ASSIGNEE(S):	Merck & Co., Inc., USA; Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.
SOURCE:	PCT Int. Appl., 19pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007130419	A2	20071115	WO 2007-US10563	20070430
WO 2007130419	A3	20081211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 2015741	A2	20090121	EP 2007-756182	20070430

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

PRIORITY APPLN. INFO.:	US 2006-797621P	P 20060504
	US 2006-832915P	P 20060724
	WO 2007-US10563	W 20070430

TI Histone deacetylase inhibitors for the treatment of neurodegeneration

IT Nervous system, disease
(Charcot-Marie-Tooth; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Brain disease
(Gilles de la Tourette syndrome; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Nervous system, disease
(Huntington's chorea; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Mental and behavioral disorders
(Pick's disease; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Brain disease
(cerebellum degeneration; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Nervous system, disease
(corticobasal degeneration; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Nervous system, disease
(dystonia musculorum deformans; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Tremor
(familial; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Eye, disease
(hereditary optic atrophy; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Alzheimer disease
Amyotrophic lateral sclerosis
Anti-Alzheimer's agents
Antiparkinsonian agents
Central nervous system agents

Creutzfeldt-Jakob disease
Drug delivery systems
Drug screening
Human
Lewy body dementia
Multiple sclerosis
Nervous system agents
Neurodegenerative disease
Parkinson's disease
Psychotropics
Retinitis pigmentosa
Stroke
(histone deacetylase inhibitors for treatment of neurodegeneration)

IT Spinal cord disease
(injury; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Nerve, disease
(neuropathy, chronic progressive; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Dementia
(pre-senile; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Paralysis
(pseudobulbar; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Dementia
(senile; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Nervous system, disease
(spinocerebellar degeneration; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Brain disease
(trauma; histone deacetylase inhibitors for treatment of neurodegeneration)

IT Dementia
(vascular; histone deacetylase inhibitors for treatment of neurodegeneration)

IT 9076-57-7, Histone deacetylase
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(HDAC; histone deacetylase inhibitors for treatment of neurodegeneration)

IT 438496-81-2, SIRT1 deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(histone deacetylase inhibitors for treatment of neurodegeneration)

IT 99-66-1, Valproic acid 183506-66-3 185517-21-9, Arundic acid 209783-80-2, MS 27-275
RL: PAC (Pharmacological activity); BIOL (Biological study)
(histone deacetylase inhibitors for treatment of neurodegeneration)

L4 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1003817 CAPLUS
DOCUMENT NUMBER: 149:246193
TITLE: Solid-phase synthesis of isotope-labeled 2-propyloctanoic acid, a therapeutic agent for stroke and Alzheimer's disease
AUTHOR(S): Ho, Jonathan Z.; Tang, Cheng; Braun, Matthew P.
CORPORATE SOURCE: Department of Drug Metabolism, Merck and Co. Inc., Rahway, NJ, 07065, USA

SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (2007), 50(5-6), 496-497
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 149:246193
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Solid-phase synthesis of isotope-labeled 2-propyloctanoic acid, a therapeutic agent for stroke and Alzheimer's disease
ST propyloctanoate carbon 13 14 solid phase synthesis symposium; anti stroke Alzheimer propyloctanoate carbon 13 14 prepn symposium
IT Alzheimer disease
Anti-Alzheimer's agents
Nervous system agents
Solid phase synthesis
Stroke
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT Carboxylic acids
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 1044754-43-9P
RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 1044754-45-1P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 106-94-5, 1-Bromopropane 106-95-6, Allyl bromide, reactions 109-52-4, Pentanoic acid, reactions 111-25-1, Hexyl bromide 124-07-2, Octanoic acid, reactions 3106-28-3, Octanoic-1-14C acid 159118-65-7, Octanoic-1,2,3,4-13C4 acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 5633-91-0P, 2-Allyloctanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 1129-37-9D, polystyrene bound
RL: RGT (Reagent); RACT (Reactant or reagent)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)
IT 99-66-1P, 2-Propylpentanoic acid 3004-93-1P, 2-Methyloctanoic acid 25234-25-7P, 2-Ethyloctanoic acid 31080-41-8P, 2-Propyloctanoic acid 1044754-42-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of carbon-13 and -14 propyloctanoate as therapeutic for stroke and Alzheimer's disease)

L4 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:703301 CAPLUS
DOCUMENT NUMBER: 147:102198
TITLE: Therapeutic agent for acute cerebral infarct
INVENTOR(S): Kajitani, Hitoshi; Funakoshi, Yosuke; Kitao, Dai

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 45pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007072902	A1	20070628	WO 2006-JP325481	20061221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1974727	A1	20081001	EP 2006-842989	20061221
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 20090203783	A1	20090813	US 2008-158331	20080620
PRIORITY APPLN. INFO.:			JP 2005-369154 A	20051222
			WO 2006-JP325481 W	20061221

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Therapeutic agent for acute cerebral infarct

AB Disclosed is a therapeutic agent for acute cerebral infarct which comprises (2R)-2-propyloctanoic acid or a salt thereof and is intended to be administered 5-72 h after the onset of symptoms. The therapeutic agent is safe and can ameliorate acute cerebral infarct or various conditions accompanied by acute cerebral infarct in a patient suffering from cerebral infarct, particularly a patient suffering from cerebral infarct who shows a score of 22 or smaller as measured according to NIH stroke scale, and therefore the therapeutic agent is useful for the treatment of acute cerebral infarct.

ST propyloctanoate injection acute cerebral infarction

IT Brain infarction
(acute; propyloctanoate for treatment of acute cerebral infarction and various conditions accompanied by infarction)

IT Mental activity
(consciousness, disorders; propyloctanoate for treatment of acute cerebral infarction and various conditions accompanied by infarction)

IT Pharmaceutical injections
(i.v. injections; propyloctanoate for treatment of acute cerebral infarction and various conditions accompanied by infarction)

IT Human
Infusion drug delivery systems
Motor skill disorders
Speech disorders
(propyloctanoate for treatment of acute cerebral infarction and various conditions accompanied by infarction)

IT 185517-21-9, (2R)-2-Propyloctanoic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(propyloctanoate for treatment of acute cerebral infarction and various conditions accompanied by infarction)

L4 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:487697 CAPLUS
DOCUMENT NUMBER: 147:132809
TITLE: Pharmacokinetics of arundic acid, an astrocyte modulating agent, in acute ischemic stroke
AUTHOR(S): Ishibashi, Hideyasu; Pettigrew, L. Creed; Funakoshi, Yosuke; Hiramatsu, Makoto
CORPORATE SOURCE: Ono Pharma USA, Inc., Lawrenceville, NJ, USA
SOURCE: Journal of Clinical Pharmacology (2007), 47(4), 445-452
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Pharmacokinetics of arundic acid, an astrocyte modulating agent, in acute ischemic stroke

AB Arundic acid is an astrocyte modulating agent that improves neurol. outcome in exptl. acute stroke models. The pharmacokinetics of arundic acid in patients with acute ischemic stroke was investigated in a randomized, double-blind study. Six groups of 8 to 9 patients each received 2, 4, 6, 8, 10, or 12 mg/kg/h of arundic acid for a daily 1-h infusion until completion of 7 doses. Maximum plasma concns. of arundic acid increased with increasing dose; however, the systemic exposure was less than dose proportional at higher doses. The mean terminal half-life was approx. 2 to 3 h. There was no excessive accumulation in plasma. Although systemic exposure in elderly patients was 30% greater than that in younger patients, the plasma concentration returned to nearly or below the limit of quantification prior to next administration. The pharmacokinetics of arundic acid in acute stroke patients assessed in this study were similar to that in healthy adults.

ST arundic acid acute ischemic stroke pharmacokinetics elderly

IT Human
Stroke
(arundic acid pharmacokinetics in acute stroke patient was similar to that in healthy adult)

IT Aging, animal
(elderly; arundic acid systemic exposure in elderly acute stroke patient was greater than that in younger patients)

IT Astrocyte
(modulator; astrocyte modulator arundic acid pharmacokinetics in acute stroke patient was similar to that in healthy adult)

IT Pharmacokinetics
(pharmacokinetics of arundic acid in acute stroke patient was similar to that in healthy adult)

IT 185517-21-9, Arundic acid
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid pharmacokinetics in acute stroke patient was similar to that in healthy adult)

L4 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:131105 CAPLUS
DOCUMENT NUMBER: 146:351131
TITLE: Expression of S100 protein and protective effect of arundic acid on the rat brain in chronic cerebral hypoperfusion
AUTHOR(S): Ohtani, Ryo; Tomimoto, Hidekazu; Wakita, Hideaki; Kitaguchi, Hiroshi; Nakaji, Kayoko; Takahashi, Ryosuke
CORPORATE SOURCE: Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, 606-8507, Japan
SOURCE: Brain Research (2007), 1135(1), 195-200
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Expression of S100 protein and protective effect of arundic acid on the rat brain in chronic cerebral hypoperfusion

AB S100 protein is expressed primarily by astroglia in the brain, and accumulates in and around the ischemic lesions. Arundic acid, a novel astroglia-modulating agent, is neuroprotective in acute cerebral infarction, whereas the protective effects remain unknown during chronic cerebral hypoperfusion. Rats undergoing chronic cerebral hypoperfusion were subjected to a bilateral ligation of the common carotid arteries, and were allowed to survive for 3, 7 and 14 days. The animals received a daily i.p. injection of 5.0, 10.0 or 20.0 mg/kg of arundic acid, or vehicle, for 14 days. Alternatively, other groups of rats received a delayed i.p. injection of 20.0 mg/kg of arundic acid or vehicle, which started from 1, 3 or 7 days after ligation and continued to 14 days. The degree of white matter (WM) lesions and the numerical d. of S100 protein-immunoreactive astroglia were estimated In the WM of rats with vehicle injections, the number of S100 protein-immunoreactive astroglia increased significantly after chronic cerebral hypoperfusion as compared to the sham-operation. A dosage of 10.0 and 20.0 mg/kg of arundic acid suppressed the numerical increase in S100 protein-immunoreactive astroglia and the WM lesions. These pathol. changes were suppressed with delayed treatment up to 7 days in terms of astroglial activation, and up to 3 days in terms of the WM lesions. The protective effects of arundic acid against WM lesions were demonstrated in a dose-dependent manner, and even after postischemic treatments. These results suggest the potential usefulness of arundic acid in the treatment of cerebrovascular WM lesions.

IT Artery
(carotid; expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

IT Brain
(cerebrum; expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

IT Astrocyte
Brain infarction
Neuroprotective agents
(expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

IT S-100 proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

IT Pharmaceutical injections
(i.p. injections; expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

IT 185517-21-9, Arundic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of S100 protein and protective effect of arundic acid on rat brain in chronic cerebral hypoperfusion)

L4 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1242136 CAPLUS
DOCUMENT NUMBER: 146:266486
TITLE: Effect of arundic acid on serum S-100β in ischemic stroke
AUTHOR(S): Pettigrew, L. Creed; Kasner, Scott E.; Gorman, Mark; Atkinson, Richard P.; Funakoshi, Yosuke; Ishibashi, Hideyasu
CORPORATE SOURCE: The Arundic Acid (ONO-2506) Stroke Study Group, Sanders-Brown Center on Aging, and Department of Neurology, University of Kentucky Medical Center, Lexington, KY, 40536-0230, USA
SOURCE: Journal of the Neurological Sciences (2006), 251(1-2), 57-61
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Effect of arundic acid on serum S-100β in ischemic stroke

AB We prospectively examined the effect of arundic acid (AA; ONO-2506) on S-100β, an astrocyte-derived protein, in a phase I acute stroke study. Subjects with acute ischemic stroke were randomized to daily infusion of AA or placebo for 7 days. Serum S-100β levels were assayed pre-infusion on Days 1-7 and post-infusion on Days 1, 3, and 7, and correlated with National Institutes of Health Stroke Scale (NIHSS). Samples were obtained from 86 subjects (46 AA, 40 placebo). Increase in S-100β protein level from baseline was less in the AA cohort than in the placebo cohort at 7 (p = 0.0471; t-test) and 12 (p = 0.0095)-hours post-infusion on Day 3. Baseline NIHSS correlated with maximal S-100β levels between Days 1 and 3 in the AA (r = 0.51; p = 0.0003) and placebo (r = 0.41; p = 0.0084) cohorts and in the pooled aggregate (n = 86; r = 0.46; p < 0.0001). The same correlations were observed between Day 10 NIHSS and Day 1-3 maximum serum S-100β levels. Treatment with AA was associated with lower serum levels of S-100β after acute ischemic stroke. Our results showing correlation between S-100β and NIHSS indicate that this protein is a clin. relevant marker of neurol. deficit in acute stroke.

ST arundic acid S 100beta ischemic stroke

IT S-100 proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-100B; arundic acid was associated with lower serum S-100β in ischemic stroke patient)

IT Human
Stroke
(arundic acid was associated with lower serum S-100β in ischemic stroke patient)

IT 185517-21-9, Arundic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid was associated with lower serum S-100β in ischemic stroke patient)

L4 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1242135 CAPLUS
DOCUMENT NUMBER: 146:266485
TITLE: Safety and tolerability of arundic acid in acute ischemic stroke
AUTHOR(S): Pettigrew, L. Creed; Kasner, Scott E.; Albers, Gregory W.; Gorman, Mark; Grotta, James C.; Sherman, David G.; Funakoshi, Yosuke; Ishibashi, Hideyasu
CORPORATE SOURCE: Stroke Program, Sanders-Brown Center on Aging, and Department of Neurology, University of Kentucky Medical Center, Lexington, KY, 40536-0230, USA
SOURCE: Journal of the Neurological Sciences (2006), 251(1-2), 50-56
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Safety and tolerability of arundic acid in acute ischemic stroke
AB Arundic acid (AA; ONO-2506), a novel modulator of astrocyte activation, may improve neuronal survival after stroke. We conducted a multicenter, dose-escalating, randomized, double-blind Phase I trial of AA in acute ischemic stroke. Subjects were randomized to treatment with AA or placebo in sequential dose tiers of 2-12 mg/kg/h (10-16 patients/group) within 24 h of stroke onset. Study drug was infused for 1 h daily over 7 days, and follow-up terminated at 40 days. Neurol. and functional outcomes were evaluated through Day 40 as exploratory endpoints. A total of 92 subjects were enrolled with no dose-related pattern of serious adverse events (AEs). Premature terminations caused by AEs occurred in four (8.2%) patients treated with AA and five (11.6%) treated with placebo. Two subjects treated with AA (4.1%) and four given placebo (9.3%) died. Exploratory efficacy anal. showed a trend toward improvement in the change from baseline National Institutes of Health Stroke Scale (NIHSS) in the 8 mg/kg/h AA group on Days 3 ($p = 0.023$ vs. placebo), 7 ($p = 0.002$), 10 ($p = 0.003$), and 40 ($p = 0.018$). A dose of 8 mg/kg/h AA produced a favorable trend in reduction of NIHSS that should be confirmed in a future clin. trial.
ST arundic acid ischemic stroke
IT Human
Stroke
(arundic acid was safe, effective and well tolerated in acute ischemic stroke patient)
IT 185517-21-9, Arundic acid
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid was safe, effective and well tolerated in acute ischemic stroke patient)

L4 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1118173 CAPLUS
DOCUMENT NUMBER: 145:460491
TITLE: Neuron-repairing compositions containing (2R)-2-propyl octanoic acid for the treatment of motion dysfunction and neural injury
INVENTOR(S): Maekawa, Hitoshi
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 41pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006290881	A	20061026	JP 2006-68509	20060314
PRIORITY APPLN. INFO.:			JP 2005-72839 A	20050315

TI Neuron-repairing compositions containing (2R)-2-propyl octanoic acid for the treatment of motion dysfunction and neural injury

AB Provide the drugs for treating effectively motor dysfunction caused by, such as the peripheral nervous system disease and nervous function disorder accompanying spinal cord injury. The drugs containing (2R)-2-Pr octanoic acid, their salts, its solvate, or those prodrugs are peripheral nervous system diseases, such as neuropathy/neuropathic diseases, the nervous function disorder by the stress of the cauda-equina nerve by spinal canal restenosis, cranial nerve paralysis, diabetic peripheral nerve disorder, the myasthenia gravis, muscular dystrophy. The oral or injection compns. can also be used to treat muscular motion dysfunction caused by the central nervous system disease, such as nervous function disorder, the disk herniation/herniated disk/hernia of intervertebral disk, the Huntington's disease, myelopathic muscular atrophy, spinocerebellar degeneration, and spinal cord injury. The compns. are useful as the prevention and treatment for those symptoms and the signs related with motion dysfunction and neural damage, for example, the peripheral neuropathy /neuropathic pain, dyskinesia, etc.

ST neuron CNS agent propyloctanoic acid motion dysfunction neural injury

IT Nervous system, disease
(Huntington's chorea; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Musculoskeletal diseases
(hernia; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Drug delivery systems
(injections; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Spinal cord, disease
(injury; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Analgesics
Central nervous system, disease
Central nervous system agents
Muscular dystrophy
Paralysis
Peripheral nervous system, disease
Spinal muscular atrophy
(neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Pain
(neuropathic pain; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Drug delivery systems
(oral; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Drug delivery systems
(powders; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

IT Drug delivery systems
(prodrugs; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for

the treatment of motion dysfunction and neural injury)
IT Artery, disease
(restenosis; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)
IT Injury
(spinal cord; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)
IT Nervous system, disease
(spinocerebellar degeneration; neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)
IT 185517-21-9, (2R)-2-Propyloctanoic acid 185517-21-9D, (2R)-2-Propyloctanoic acid, salts and solvates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuron-repairing compns. containing (2R)-2-Pr octanoic acid for the treatment of motion dysfunction and neural injury)

L4 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:946669 CAPLUS
DOCUMENT NUMBER: 146:453637
TITLE: Could treatment with arundic acid (ONO-2506) increase vulnerability for depression?
AUTHOR(S): Manev, Radmila; Manev, Hari
CORPORATE SOURCE: Department of Psychiatry and the Psychiatric Institute, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Medical Hypotheses (2006), 67(5), 1170-1172
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A review. Arundic acid (ONO-2506) is believed to be neuroprotective because of its actions on glia cells; i.e., its inhibitory effects on the synthesis of a calcium-binding protein S100B. ONO-2506 is undergoing clin. trials for the treatment of patients with stroke and Alzheimer's disease. Recent clin. studies point to a pervasive comorbidity of depression with stroke and Alzheimer's disease. Previously, S100B has been implicated in the pathobiol. mechanisms of depression. Preclin. studies have shown that antidepressant treatment significantly increases brain S100B. Here we hypothesize that available data that link S100B with depression, along with the proposed inhibitory action of ONO-2506 on S100B synthesis, indicate that this compound could increase vulnerability for depression in patients at risk for this disorder, and we propose that evaluation of patients with stroke and Alzheimer's disease for the presence of depression should be routine in clin. trials employing ONO-2506. Although it may be open for discussion whether the neuroprotective effects of ONO-2506 are exclusively due to its inhibition of S100B synthesis, the latter action of ONO-2506 warrants studies of the effects of this drug in the pathobiol. of depression.
ST review arundic acid depression stroke Alzheimer disease
IT S-100 proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-100B; arundic acid inhibits synthesis of calcium-binding protein S100B that could increase vulnerability for depression in patient with stroke and Alzheimer's disease)
IT Alzheimer disease
Depression

Human
Neuroprotective agents
Stroke
(arundic acid inhibits synthesis of calcium-binding protein S100B that could increase vulnerability for depression in patient with stroke and Alzheimer's disease)

IT 185517-21-9, Arundic acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid inhibits synthesis of calcium-binding protein S100B that could increase vulnerability for depression in patient with stroke and Alzheimer's disease)

L4 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:777622 CAPLUS
DOCUMENT NUMBER: 145:224763
TITLE: Arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice
AUTHOR(S): Mori, Takashi; Town, Terrence; Tan, Jun; Yada, Nobumichi; Horikoshi, Yuko; Yamamoto, Junki; Shimoda, Taiji; Kamanaka, Yoshihisa; Tateishi, Narito; Asano, Takao
CORPORATE SOURCE: Institute of Medical Science, Saitama Medical School, Kawagoe, Saitama, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2006), 318(2), 571-578
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice

AB Like microglia, reactive astrocytes produce a myriad of neurotoxic substances in various brain pathologies, such as Alzheimer's disease (AD), trauma, and cerebral ischemia. Among the numerous products of reactive astrocytes, attention has recently been directed toward the possible detrimental role of S100B, because the protein has been shown to be highly expressed along with the progression of brain damage and to exert neurotoxic effects at high concns. The present study aimed to examine the possible role of astrocyte-derived S100B in the progression of cerebral amyloidosis and gliosis in transgenic mice overproducing mutant amyloid precursor protein (Tg APPsw mice, line 2576). For this purpose, arundic acid (Ono Pharmaceutical Co., Ltd., Mishima, Osaka, Japan), which is known to neg. regulate astrocyte synthesis of S100B, was orally administered to Tg APPsw mice for 6 mo from 12 mo of age, and the effects of the agent on the above parameters were examined Here, we report that β-amyloid deposits along with amyloid-β peptide/S100B levels, as well as β-amyloid plaque-associated reactive gliosis (astrocytosis and microgliosis), were significantly ameliorated in arundic acid-treated Tg APPsw mice relative to vehicle-treated Tg APPsw mice at 19 mo of age. Based on the above results, arundic acid is considered to deserve further exploration as a promising therapeutic agent for AD.

IT Calcium-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-100B; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)

IT Brain, disease

(amyloidosis; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Alzheimer's disease
Anti-Alzheimer's agents
Astrocyte
(arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Amyloid precursor proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Astrocyte
(astrocytosis; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Amyloidosis
(cerebral; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Neuroglia, disease
(gliosis; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Neuroglia
(microglia; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT Amyloid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)
IT 185517-21-9, Arundic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid ameliorates cerebral amyloidosis and gliosis in Alzheimer transgenic mice)

L4 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:626131 CAPLUS
DOCUMENT NUMBER: 145:116338
TITLE: Role of the astrocyte-specific protein S100B in acute stroke
AUTHOR(S): Shinagawa, Rika; Shimoda, Taiji; Kagamiishi, Yoshifumi; Kamanaka, Yoshihisa
CORPORATE SOURCE: Res. Div., Ono Pharmaceutical Co., Ltd., Osaka, 618-8585, Japan
SOURCE: Nippon Yakurigaku Zasshi (2006), 127(6), 485-488
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
TI Role of the astrocyte-specific protein S100B in acute stroke
AB A review on roles of brain ischemia-induced astrocyte activation and astrocyte-specific S100B in acute stroke, and neuroprotective action mechanism of arundic acid (ONO-2506) through inhibiting astrocyte activation and S100B formation.
ST review astrocyte S100B stroke; arundic acid neuroprotectant astrocyte S100B inhibition review
IT Calcium-binding proteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,

unclassified); BIOL (Biological study)
(S-100B; astrocyte-specific protein S100B in acute stroke and action mechanism of neuroprotective arundic acid)
IT Astrocyte
(astrocyte-specific protein S100B in acute stroke and action mechanism of neuroprotective arundic acid)
IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; astrocyte-specific protein S100B in acute stroke and action mechanism of neuroprotective arundic acid)
IT Brain, disease
(stroke; astrocyte-specific protein S100B in acute stroke and action mechanism of neuroprotective arundic acid)
IT 185517-21-9, Arundic acid
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(astrocyte-specific protein S100B in acute stroke and action mechanism of neuroprotective arundic acid)

L4 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:541123 CAPLUS
DOCUMENT NUMBER: 144:495432
TITLE: Drugs containing (2R)-2-propyloctanoic acid and other active agents for treatment of neurodegenerative disease
INVENTOR(S): Tateishi, Shigeto; Shimoda, Taiji; Shinagawa, Rika
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006143708	A	20060608	JP 2005-302476	20051018
PRIORITY APPLN. INFO.:			JP 2004-304933 A	20041019

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

IT Brain, disease
(infarction; drugs containing (2R)-2-propyloctanoic acid and other active agents for treatment of neurodegenerative disease)
IT Nerve regeneration
(promoters; drugs containing (2R)-2-propyloctanoic acid and other active agents for treatment of neurodegenerative disease)
IT 185517-21-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug synergist; drugs containing (2R)-2-propyloctanoic acid and other active agents for treatment of neurodegenerative disease)

L4 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:494188 CAPLUS
DOCUMENT NUMBER: 145:7747
TITLE: Preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke
INVENTOR(S): Munoz, Benito; Payne, Joseph E.; Prasit, Petpiboon; Reger, Thomas S.; Smith, Nicholas D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006055381	A2	20060526	WO 2005-US40727	20051110
WO 2006055381	A3	20060803		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005306741	A1	20060526	AU 2005-306741	20051110
CA 2587040	A1	20060526	CA 2005-2587040	20051110
EP 1814838	A2	20070808	EP 2005-851501	20051110
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101056842	A	20071017	CN 2005-80038863	20051110
JP 2008520569	T	20080619	JP 2007-541311	20051110
IN 2007CN01651	A	20070831	IN 2007-CN1651	20070423
US 20080132488	A1	20080605	US 2007-667814	20070515
US 7495029	B2	20090224		
KR 2007085379	A	20070827	KR 2007-711132	20070516
PRIORITY APPLN. INFO.:			US 2004-628280P P	20041116
			WO 2005-US40727 W	20051110

OTHER SOURCE(S): CASREACT 145:7747; MARPAT 145:7747
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke

AB Prodrugs of (2R)-2-propyloctanoic acid, and pharmaceutical comps. comprising them, which may be effective in modulating multiple events in the biochem. cascade of stroke are prepared.

IT Carboxylic acids, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chiral; preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT Carboxylic acids, preparation
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters; in the preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT Esterification
(in the preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT Drug delivery systems
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke in)

IT Brain, disease
(stroke; preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 1310-65-2, Lithium hydroxide 185517-21-9,

(2R)-2-Propyloctanoic acid 888010-84-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(in the preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 888038-78-6P, Lithium (2R)-2-propyloctanoate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in the preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 76-05-1, Trifluoroacetic acid, reactions 513-35-9, 2-Methyl-2-butene 2758-06-7, (2-Bromoethyl)trimethylammonium bromide 18162-48-6, tert-Butyldimethylsilyl chloride 103745-39-7, Fasudil 179174-80-2 180001-34-7, 1400-W
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 885020-48-4P 888010-86-4P 888010-87-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 70-11-1P, 2-Bromoacetophenone 888010-85-3P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 32001-55-1, Pyridinium fluoride
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

IT 888010-88-6P 888010-90-0P 888010-91-1P 888010-92-2P 888010-93-3P 888010-94-4P 888010-95-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of prodrugs of (2R)-2-propyloctanoic acid for the treatment of stroke)

L4 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:383645 CAPLUS
DOCUMENT NUMBER: 144:382019
TITLE: Therapeutic agent for Parkinson's disease
INVENTOR(S): Tateishi, Narito; Satoh, Souich; Shimoda, Taiji; Shinagawa, Rika; Abe, Shinichiro; Morimoto, Masao; Mizushima, Ken; Fujii, Akifumi; Kagamiishi, Yoshifumi
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006043532	A1	20060427	WO 2005-JP19092	20051018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,				

YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-304934 A 20041019
JP 2005-59904 A 20050304

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Brain
(cerebral function activators; therapeutic agents for Parkinson's disease containing (2R)-2-propyloctanoic acid with/without of other active agents)

IT 59-92-7, Levodopa, biological studies 322-35-0, Benserazide 22260-51-1, Bromocriptine mesylate 28860-95-9, Carbidopa 37270-69-2, Levodopa-benserazide mixt 57308-51-7, Carbidopa-levodopa mixture 185517-21-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for Parkinson's disease containing (2R)-2-propyloctanoic acid with/without of other active agents)

L4 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:309639 CAPLUS
DOCUMENT NUMBER: 145:499861
TITLE: 1,026 Experimental treatments in acute stroke
AUTHOR(S): O'Collins, Victoria E.; Macleod, Malcolm R.; Donnan, Geoffrey A.; Horky, Laura L.; van der Worp, Bart H.; Howells, David W.
CORPORATE SOURCE: Neuroscience Lab, Department of Medicine, Austin Health, University of Melbourne, Heidelberg, Australia
SOURCE: Annals of Neurology (2006), 59(3), 467-477
CODEN: ANNED3; ISSN: 0364-5134
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 69 THERE ARE 69 CAPLUS RECORDS THAT CITE THIS RECORD (69 CITINGS)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI 1,026 Experimental treatments in acute stroke

AB Objective: Preclin. evaluation of neuroprotectants fostered high expectations of clin. efficacy. When not matched, the question arises whether expts. are poor indicators of clin. outcome or whether the best drugs were not taken forward to clin. trial. Therefore, we endeavored to contrast exptl. efficacy and scope of testing of drugs used clin. and those tested only exptl. Methods: We identified neuroprotectants and reports of exptl. efficacy via a systematic search. Controlled in vivo and in vitro expts. using functional or histol. end points were selected for anal. Relationships between outcome, drug mechanism, scope of testing, and clin. trial status were assessed statistically. Results: There was no evidence that drugs used clin. (114 drugs) were more effective exptl. than those tested only in animal models (912 drugs), for example, improvement in focal models averaged 31.3±16.7% vs. 24.4±32.9%, $p > 0.05$, resp. Scope of testing using Stroke Therapy Academic Industry Roundtable (STAIR) criteria was highly variable, and no relationship was found between mechanism and efficacy. Interpretation: The results question whether the most efficacious drugs are being selected for stroke clin. trials. This may partially explain the slow progress in developing treatments. Greater rigor in the conduct, reporting, and anal. of animal data will improve the transition

of scientific advances from bench to bedside.

ST neuroprotectant brain stroke ischemia

IT Anti-inflammatory agents
(STAIR criteria indicated no evidence that neuroprotective drugs including antiinflammatory used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Antioxidants
(STAIR criteria indicated no evidence that neuroprotective drugs including antioxidant used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Hypothermia
(STAIR criteria indicated no evidence that neuroprotective drugs including hypothermia used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Antihypertensives
β-Adrenoceptor antagonists
(STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Thrombolytics
(STAIR criteria indicated no evidence that neuroprotective drugs including thrombolytic used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Human
(STAIR criteria was highly variable but no link between mechanism and efficacy indicated no evidence that neuroprotectants used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Natural products, pharmaceutical
(Salviae miltiorrhizae radix; STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Ischemia
(cerebral; STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Brain, disease
(ischemia; STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; STAIR criteria was highly variable but no link between mechanism and efficacy indicated no evidence that neuroprotectants used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT Brain, disease
(stroke; STAIR criteria was highly variable but no link between mechanism and efficacy indicated no evidence that neuroprotectants used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT 106096-93-9, Basic fibroblast growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT 50-02-2, Dexamethasone 50-78-2, Aspirin 53-86-1, Indomethacin 55-63-0, Nitroglycerin 56-40-6, Glycine, biological studies 56-81-5, Glycerol, biological studies 58-74-2, Papaverine 69-65-8, D-Mannitol 89-25-8, MCI-186 103-90-2, Paracetamol 125-73-5, Dextrorphan 127-31-1, Fludrocortisone 317-34-0, Aminophylline 322-79-2, Triflusal 437-74-1 439-14-5, Diazepam 456-59-7, Cyclandelate 465-65-6, Naloxone 525-66-6, Propranolol 533-45-9, Clomethiazole 987-78-0, Citicoline 1134-47-0, Baclofen 3200-06-4, Nafronyl oxalate 6493-05-6, Pentoxifylline 7487-88-9, Magnesium sulfate, biological studies 7491-74-9, Piracetam 8067-24-1, Hydergine 9002-01-1, Streptokinase 9002-60-2, Corticotrophin, biological studies 9004-10-8, Insulin, biological studies 9004-54-0, Dextran, biological studies 9005-27-0, Pentastarch 9039-53-6, Urokinase 9039-61-6, Batroxobin 11096-26-7, Erythropoietin 12656-61-0, Cerebrolysin 24967-93-9, Org 10172 25332-39-2, Desyrel 27848-84-6, Nicergoline 29122-68-7, Atenol 35121-78-9, Prostacyclin 36702-83-7, Tinofedrine 42971-09-5, Vinpocetine 52468-60-7, Flunarizine 55096-26-9, Nalmefene 55242-55-2, Propentofylline 55985-32-5, Nicardipine 60940-34-3, Ebselen 66085-59-4, Nimodipine 72803-02-2, PY 108-068 74863-84-6, Argatroban 79455-30-4, Nicaraven 79902-63-9, Simvastatin 80714-61-0, Semax 82657-92-9, Prourokinase 83712-60-1, Defibrotide 93390-81-9, Fosphenytoin 104443-62-1, Ganglioside GM1 104987-11-3, FK506 105857-23-6, Alteplase 110101-66-1, Tirilazad 110347-85-8, CGS 19755 119431-25-3, Eliprodil 119514-66-8, Lifarizine 122933-57-7, Tanakan (platelet-activating factor-acether antagonist) 128298-28-2, Remacemide 130800-90-7, Sipatrigine 131094-16-1, Fiblast 137160-11-3, Cerestat 142864-19-5, Enlimomab 143653-53-6, Abciximab 144494-65-5, Tirofiban 144665-07-6, Lubeluzole 144980-29-0, Repinotan 145040-37-5, Candesartan cilexetil 145137-38-8, Desmoteplase 153322-05-5, ARL 15896 153436-22-7, Gavestinel 153504-81-5, Licostinel 154164-30-4, YM90K 156756-10-4, TAK-218 161605-73-8, ZK200775 162117-90-0, S-0139 168021-79-2, NXY-059 185517-21-9, ONO-2506 186495-99-8, NPS 1506 187523-35-9, BMS-204352 188591-67-5, CP 101606-27 188627-80-7, Eptifibatide 191588-94-0, Tenecteplase 205510-69-6, RPR 109891 210245-80-0, YM872 211866-70-5, PS519 221019-25-6, BIII 890 222315-88-0, DP-b99 245063-59-6, NS1209 339086-79-2, LeukArrest 339164-13-5, LDP 01 474877-20-8, Neutrophil inhibitory factor 679809-58-6, Enoxaparin sodium 823805-47-6, Caffeinol 915091-64-4, S 1746
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT 9005-49-6, Certoparin, biological studies
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparin; STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

IT 7782-44-7, Oxygen, biological studies
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hyperbaric; STAIR criteria indicated no evidence that neuroprotective drugs including radix salviae miltiorrhizae used in acute stroke patient were more effective exptl. than those tested in hamster model of focal ischemia)

L4 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:48593 CAPLUS

DOCUMENT NUMBER: 144:135154
TITLE: Prodrugs for (optically active) 2-propyloctanoic acid, their compositions for improving astrocyte function, and prevention and/or treatment of neurodegenerative disease with the prodrugs
INVENTOR(S): Nakayama, Kosuke
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006016319	A	20060119	JP 2004-193923	20040630
PRIORITY APPLN. INFO.:			JP 2004-193923	20040630

OTHER SOURCE(S): MARPAT 144:135154
IT Circulation
(cerebral, improvers; propyloctanoic acid prodrugs with improved pharmacokinetics for improving astrocyte function and treatment of neurodegenerative disease and their use in combination with other drugs)
IT 31080-41-8, 2-Propyloctanoic acid 185517-21-9, (2R)-2-Propyloctanoic acid
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(propyloctanoic acid prodrugs with improved pharmacokinetics for improving astrocyte function and treatment of neurodegenerative disease and their use in combination with other drugs)

L4 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:25443 CAPLUS
DOCUMENT NUMBER: 144:266572
TITLE: Teratogenic effects mediated by inhibition of histone deacetylases evidence from quant. structure activity relationships of valproic acid derivs.
AUTHOR(S): Eikel, Daniel; Lampen, Alfonso; Nau, Heinz
CORPORATE SOURCE: Department of Food Toxicology and Chemical Analysis-Food Toxicology, Center for Systemic Neuroscience Hannover, Center for Food Science, University of Veterinary Medicine Hannover, Hannover, D-30173, Germany
SOURCE: Chemical Research in Toxicology (2006), 19(2), 272-278
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The widely used antiepileptic drug valproic acid (VPA), which is also used in migraine prophylaxis and the treatment of bipolar disorders, is also under trial as an anticancer agent. Despite its wide range of therapeutic applications, VPA also has two severe side effects: acute liver toxicity and teratogenicity. The mechanism of action for all these properties is unknown to date, but recently, it was shown that VPA is able to inhibit the enzyme class of histone deacetylases (HDACs), proteins with a fundamental impact on gene expression and therefore possible mol. targets of VPA-induced signaling cascades. The purpose of this study was to determine

if teratogenic side effects of VPA could be linked to its HDAC inhibition ability by studying a large set of structurally diverse derivs. based on the VPA core structure. We demonstrate that only VPA derivs. with a teratogenic potential in mice are able to induce a hyperacetylation in core histone H4 in teratocarcinoma F9 cells. We also demonstrate that this marker of functional HDAC inhibition occurs almost immediately (15 min) after exposure of F9 cells to VPA, whereas no influence on the HDAC protein levels (HDAC 2 and HDAC 3) could be detected even after 24 h of treatment. Further measurement of the IC50(HDAC) values of VPA derivs. in a human HDAC enzyme test system revealed an activity range from 10 to 10 000 μM; in some derivs., HDAC inhibition ability was 40 times that of VPA. We also show a quant. correlation between the IC50(HDAC) and the teratogenic potential of VPA derivs., which clearly points toward HDACs as the formerly described teratogenic receptors of VPA-induced neural tube defects (NTDs).

IT Nervous system, disease
(neural tube defect; valproic acid derivs. quant. structure activity relationships and its teratogenic side effects mediated by inhibition of histone deacetylases)

IT 108-81-6 1575-72-0 2430-27-5, Valpromide 3274-28-0 3639-22-3 5662-78-2 31080-39-4 31080-41-8 33786-47-9 51577-99-2 59726-46-4 96017-59-3 106132-78-9 155899-34-6 155899-35-7 176638-49-6 176638-59-8 178447-22-8 675831-45-5 675831-46-6
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(valproic acid derivs. quant. structure activity relationships and its teratogenic side effects mediated by inhibition of histone deacetylases)

L4 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1328560 CAPLUS
DOCUMENT NUMBER: 144:57565
TITLE: Capsule stable against mastication
INVENTOR(S): Okamoto, Ichiro; Miyamoto, Yuji; Nishimura, Hidekatsu
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005120490	A1	20051222	WO 2005-JP11092	20050610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005251623	A1	20051222	AU 2005-251623	20050610
CA 2569746	A1	20051222	CA 2005-2569746	20050610
EP 1754479	A1	20070221	EP 2005-751213	20050610
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

CN 101001622	A	20070718	CN 2005-80027281		20050610
BR 2005012000	A	20080122	BR 2005-12000		20050610
MX 2006014396	A	20070312	MX 2006-14396		20061208
NO 2006005670	A	20070312	NO 2006-5670		20061208
ZA 2006010307	A	20080730	ZA 2006-10307		20061208
IN 2006CN04534	A	20070629	IN 2006-CN4534		20061211
US 20080057115	A1	20080306	US 2006-629178		20061211
KR 2007024722	A	20070302	KR 2007-700705		20070111
PRIORITY APPLN. INFO.:			JP 2004-174576	A	20040611
			JP 2005-122821	A	20050420
			WO 2005-JP11092	W	20050610

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Nerve, disease
Nerve regeneration
(soft capsules stable against mastication containing propyloctanoate for treatment of nerve disorders)

IT 185517-21-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soft capsules stable against mastication containing propyloctanoate for treatment of nerve disorders)

L4 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1196407 CAPLUS
DOCUMENT NUMBER: 143:459776
TITLE: Preparation of crystal comprising (2R)-2-propyloctanoic acid and amine
INVENTOR(S): Hasegawa, Tomoyuki; Kawanaka, Yasufumi; Kasamatsu, Eiji
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105722	A1	20051110	WO 2005-JP8462	20050427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1741697	A1	20070110	EP 2005-739057	20050427
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			JP 2004-134655	A 20040428
			WO 2005-JP8462	W 20050427

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Nerve, disease
Nerve regeneration
Nervous system agents
(reparation of crystalline (2R)-2-propyloctanoic acid amine salts as preventives, therapeutic agents, and/or symptom-suppressing agents for neurodegenerative diseases, nerve disorders, or diseases required for neuroregeneration)

IT 185517-21-9P 807362-89-6P 807362-94-3P 807362-99-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reparation of crystalline (2R)-2-propyloctanoic acid amine salts as preventives, therapeutic agents, and/or symptom-suppressing agents for neurodegenerative diseases, nerve disorders, or diseases required for neuroregeneration)

IT 548783-50-2P
RL: PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reparation of crystalline (2R)-2-propyloctanoic acid amine salts as preventives, therapeutic agents, and/or symptom-suppressing agents for neurodegenerative diseases, nerve disorders, or diseases required for neuroregeneration)

IT 868587-88-6P 869109-74-0P 869109-77-3P
869109-78-4P 869109-79-5P 869109-80-8P
869109-81-9P 869109-82-0P 869109-83-1P
869109-84-2P 869109-85-3P 869109-87-5P
869109-88-6P 869109-89-7P 869109-91-1P
869109-92-2P 869109-93-3P 869109-94-4P
869109-95-5P 869109-97-7P 869109-98-8P
869109-99-9P 869110-00-9P 869110-01-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reparation of crystalline (2R)-2-propyloctanoic acid amine salts as preventives, therapeutic agents, and/or symptom-suppressing agents for neurodegenerative diseases, nerve disorders, or diseases required for neuroregeneration)

IT 869109-75-1P 869109-76-2P 869109-86-4P
869109-96-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reparation of crystalline (2R)-2-propyloctanoic acid amine salts as preventives, therapeutic agents, and/or symptom-suppressing agents for neurodegenerative diseases, nerve disorders, or diseases required for neuroregeneration)

L4 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:553303 CAPLUS
DOCUMENT NUMBER: 143:109607
TITLE: Modulation of astrocytic activation by arundic acid (ONO-2506) mitigates detrimental effects of the apolipoprotein E4 isoform after permanent focal ischemia in apolipoprotein E knock-in mice
AUTHOR(S): Mori, Takashi; Town, Terrence; Tan, Jun; Tateishi, Narito; Asano, Takao
CORPORATE SOURCE: Institute of Medical Science, Saitama Medical Center/School, Saitama, Japan
SOURCE: Journal of Cerebral Blood Flow & Metabolism (2005), 25(6), 748-762
CODEN: JCBMDN; ISSN: 0271-678X
PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Using homozygous human apolipoprotein E2 (apoE2) (2/2)-, apoE3 (3/3)-, or apoE4 (4/4)-knock-in (KI) mice, we have shown that delayed infarct expansion and reactive astrocytosis after permanent middle cerebral artery occlusion (pMCAO) were markedly exacerbated in 4/4-KI mice as compared with 2/2- or 3/3-KI mice. Here, we probed the putative causal relationship between enhanced astrocytic activation and exacerbation of brain damage in 4/4-KI mice using arundic acid (ONO-2506, Ono Pharmaceutical Co. Ltd), which is known to oppose astrocytic activation through its inhibitory action on S100B synthesis. In all of the KI mice, administration of arundic acid (10 mg/kg day, i.p., started immediately after pMCAO) induced significant amelioration of brain damage at 5 days after pMCAO in terms of infarct vols. (results expressed as the mean infarct volume (mm3) ± 1 s.d. in 2/2-, 3/3-, or 4/4-KI mice in the vehicle groups: 16 ± 2, 15 ± 2, or 22 ± 2; in the arundic acid groups: 11 ± 2 ($P < 0.001$), 11 ± 2 ($P < 0.001$), or 12 ± 2 ($P < 0.001$), as compared with the vehicle groups), neurol. deficits, and S100/glial fibrillary acidic protein burden in the peri-infarct area. The beneficial effects of arundic acid were most pronounced in 4/4-KI mice, wherein delayed infarct expansion together with deterioration of neurol. deficits was almost completely mitigated. The above results support the notion that the apoE4 isoform exacerbates brain damage during the subacute phase of pMCAO through augmentation of astrocytic activation. Thus, pharmacol. modulation of astrocytic activation may confer a novel therapeutic strategy for ischemic brain damage, particularly in APOE ε4 carriers.

IT Calcium-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-100B; arundic acid decreased immunoreactivity and tissue level of S100 protein burden in astrocytes of peri-infarct area after permanent middle cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT Astrocyte
(arundic acid markedly attenuated magnitude of reactive astrocytosis in brain after permanent middle cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT Glial fibrillary acidic protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(arundic acid significantly attenuated glial fibrillary acidic protein burden after permanent middle cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT Brain
(arundic acid significantly reduced infarct volume and area and thus ameliorated brain damage after permanent middle cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT Astrocyte
(astrocytosis; arundic acid markedly attenuated magnitude of reactive astrocytosis in brain after permanent middle cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT Ischemia
(cerebral; arundic acid reduced infarct volume, area, improved neurol. deficits, decreased immunoreactivity, tissue level of S100 and GFAP protein, attenuated astrocytic activation after permanent focal ischemia in apo E isoform knock-in mouse)

IT Brain, disease
(infarction; arundic acid significantly reduced infarct volume and area and thus ameliorated brain damage after permanent middle

cerebral artery occlusion in apolipoprotein E isoform knock-in mouse)

IT 185517-21-9, Arundic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arundic acid reduced infarct volume, area, improved neurol. deficits, decreased immunoreactivity and tissue level of S100 and GFAP protein burden, attenuated astrocytic activation after pMCAO in apolipoprotein E isoform knock-in mouse)

L4 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:371949 CAPLUS
DOCUMENT NUMBER: 143:108756
TITLE: Arundic acid (ONO-2506) ameliorates delayed ischemic brain damage by preventing astrocytic overproduction of S100B
AUTHOR(S): Asano, T.; Mori, T.; Shimoda, T.; Shinagawa, R.; Satoh, S.; Yada, N.; Katsumata, S.; Matsuda, S.; Kagamiishi, Y.; Tateishi, N.
CORPORATE SOURCE: Department of Neurosurgery, Saitama Medical Center/ School, Saitama, 350-8550, Japan
SOURCE: Current Drug Targets: CNS & Neurological Disorders (2005), 4(2), 127-142
CODEN: CDTCCC; ISSN: 1568-007X
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 238 THERE ARE 238 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. After focal cerebral ischemia, the infarct volume increases rapidly within acute infarct expansion (initial 12 to 24 h) and continues slowly during delayed infarct expansion (25 to 168 h). While acute infarct expansion represents progressive necrosis within the ischemic core, delayed infarct expansion starts as disseminated apoptotic cell death in a narrow rim surrounding the infarct border, which gradually coalesces to form a larger infarct. Discovery of a distinct correlation between reactive astrogliosis along the infarct border and delayed infarct expansion in the rodent ischemia model led us to investigate the possible causal relation between the two events. Specifically, the calcium binding protein S100B exerts detrimental effects on cell survival through activation of various intracellular signaling pathways, resulting in altered protein expression. Arundic acid [(R)-(-)-2-propyloctanoic acid, ONO-2506] is a novel agent that inhibits S100B synthesis in cultured astrocytes. In the rodent ischemia model, this agent was shown to inhibit both the astrocytic overexpression of S100B and the subsequent activation of signaling pathways in the peri-infarct area. Concurrently, delayed infarct expansion was prevented, and neurol. deficits were promptly ameliorated. The results of subsequent studies suggest that the efficacy of arundic acid is mediated by restoring the activity of astroglial glutamate transporters via enhanced genetic expression.

IT Injury
Ischemia
(cerebral; arundic acid ameliorates delayed ischemic brain damage by preventing astrocytic overprodn. of S100B)

IT Brain, disease
(infarction; arundic acid ameliorates delayed ischemic brain damage by preventing astrocytic overprodn. of S100B)

IT 185517-21-9, Arundic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(arundic acid ameliorates delayed ischemic brain damage by preventing astrocytic overprodn. of S100B)

L4 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:316347 CAPLUS
DOCUMENT NUMBER: 142:349089
TITLE: Method for preventing and/or treating neurodegenerative diseases
INVENTOR(S): Funakoshi, Yosuke; Mizushima, Ken; Takakuwa, Toshio
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005032537	A1	20050414	WO 2004-JP14893	20041001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1667672	A1	20060614	EP 2004-773691	20041001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007507490	T	20070329	JP 2006-531234	20041001
US 20070043116	A1	20070222	US 2006-574489	20060725
PRIORITY APPLN. INFO.:			US 2003-507952P P	20031003
			JP 2004-174577 A	20040611
			WO 2004-JP14893 W	20041001

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The invention relates to a neurodegenerative disease treating agent for parenteral use, which comprises (2R)-2-propyloctanoic acid or a salt thereof. Since the neurodegenerative disease treating agent of the invention comprising (2R)-2-propyloctanoic acid or a salt thereof, characterized in that a dosage exceeding 100 mg per dose is parenterally administered, shows neuropathy improving effect and S-100 β increase inhibiting effect in patients with cerebral infarction , it is useful for the treatment of neurodegenerative diseases including cerebral infarction. In addition, it is also useful as a neural regeneration agent after transplantation.

ST propyloctanoic acid neurodegenerative disease therapy neural regeneration

IT Brain, disease
(infarction; method for prevention and treatment of neurodegenerative diseases)

IT Regeneration, animal
(neural; method for prevention and treatment of neurodegenerative diseases)

IT Brain, disease
(stroke; method for prevention and treatment of neurodegenerative diseases)
IT 185517-21-9
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for prevention and treatment of neurodegenerative diseases)

L4 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:316345 CAPLUS
DOCUMENT NUMBER: 142:379379
TITLE: Nerve regeneration promoters containing fatty acid compounds
INVENTOR(S): Tateishi, Narito; Yamamoto, Junki; Kawaharada, Soichi; Akiyama, Tsutomu; Hoshikawa, Masamitsu
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005032535	A1	20050414	WO 2004-JP14879	20041001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1685832	A1	20060802	EP 2004-792173	20041001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 20070043114	A1	20070222	US 2006-574479	20061005
PRIORITY APPLN. INFO.:			JP 2003-345123 A	20031003
			JP 2004-162909 A	20040601
			WO 2004-JP14879 W	20041001

OTHER SOURCE(S): MARPAT 142:379379
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Nerve regeneration promoters containing fatty acid compounds
AB Disclosed are nerve regeneration promoters containing fatty acid compds. especially compds. R2C(R3)(R4)COR1 [R1 hydroxy; R2, R3 = H, C1, C3-10 alkyl, C3-10 alkenyl, etc.; R4 = (oxidized) C2-3 alkyl], salts thereof or prodrugs of the same. The compds. inhibit nerve cell death and promote the formation of new nerve cells and nerve cell regeneration and also promote the repair and regeneration of nerve tissues and functions through neurite extension, because of serving as a stem cell (nerve stem cell, embryonic stem cell, bone marrow cell, etc.) proliferation/differentiation promoter, a nerve cell precursor proliferation/differentiation promoter, a neurotrophic factor activity enhancer, a neurotrophic factor-like substance or a neurodegeneration inhibitor. Furthermore, these compds. are

useful in preparing cells for transplantation (nerve stem cells, nerve cell precursors, nerve cells, etc.) from a brain tissue, bone marrow, embryonic stem cells, etc. At the same time, these compds. promote the take, proliferation, differentiation and function expression of transplanted cells, which makes them useful as preventives and/or remedies for neurodegenerative diseases. The effect of (2R)-2-propyloctanoic acid on nerve stem cell differentiation in rats was examined

ST fatty acid compd nerve regeneration promoter; propyloctanoic acid nerve regeneration promoter

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; nerve regeneration promoters containing fatty acid compds.)

IT Nerve
(central; nerve regeneration promoters containing fatty acid compds.)

IT Prosthetic materials and Prosthetics
(implants; nerve regeneration promoters containing fatty acid compds.)

IT Drug delivery systems
(injections; nerve regeneration promoters containing fatty acid compds.)

IT Nerve
(motor; nerve regeneration promoters containing fatty acid compds.)

IT Animal tissue culture
Astrocyte
Brain
Cell differentiation
Cell proliferation
Mesenchyme
Nerve regeneration
Nerve regeneration
Neuroglia
Stem cell
(nerve regeneration promoters containing fatty acid compds.)

IT Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nerve regeneration promoters containing fatty acid compds.)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nerve regeneration promoters containing fatty acid compds.)

IT Nerve
(peripheral; nerve regeneration promoters containing fatty acid compds.)

IT Nerve
(sensory; nerve regeneration promoters containing fatty acid compds.)

IT Nerve
(spinal; nerve regeneration promoters containing fatty acid compds.)

IT Neuron
(stem cells, precursor cells; nerve regeneration promoters containing fatty acid compds.)

IT Bone marrow
Embryo, animal
(stem cells; nerve regeneration promoters containing fatty acid compds.)

IT Cell
(stromal, bone marrow; nerve regeneration promoters containing

fatty acid compds.)
IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(unsatd.; nerve regeneration promoters containing fatty acid compds.)
IT 99-66-1, 2-Propylpentanoic acid 31080-41-8, 2-Propyloctanoic acid 185517-21-9, (2R)-2-Propyloctanoic acid 807363-10-6 824961-07-1 824961-08-2 824961-09-3 824961-10-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nerve regeneration promoters containing fatty acid compds.)

L4 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:65515 CAPLUS
DOCUMENT NUMBER: 143:306237
TITLE: Asymmetric approach to (R)-(-)-2-propyloctanoic acid
AUTHOR(S): Roos, Gregory H. P.; Al Kalbani, Rayan; Al Ajmi, Huda
CORPORATE SOURCE: Chemistry Department, Sultan Qaboos University, Al Khoud, 123, Oman
SOURCE: Journal of Saudi Chemical Society (2004), 8(3), 485-489
CODEN: JSCSFO; ISSN: 1319-6103
PUBLISHER: Saudi Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:306237
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB In an attempt to improve crystallinity of intermediates, a chiral imidazolidin-2-one auxiliary was tested in the standard diastereoselective allylation approach to the formal synthesis of (R)-2-propyloctanoic acid, which has been reported as a potential therapeutic agent for stroke and Alzheimer's disease. Allyl intermediate I was only semi-crystalline, while the corresponding propargyl intermediate defied crystallization
Hydrogenation of I and cleavage of the auxiliary gave the title compound in only 85% optical purity, implying that some racemization had occurred during the hydrogenation and hydrolysis steps.
IT 185517-21-9P, (R)-(-)-2-Propyloctanoic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of (R)-propyloctanoic acid via fusion of (+)-ephedrine with urea followed by asym. alkylation with allyl bromide or propargyl bromide, hydrogenation, and hydrolysis in the attempt to prepare crystalline intermediates)

L4 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:765918 CAPLUS
DOCUMENT NUMBER: 142:168553
TITLE: Arundic Acid: Astrocyte-modulating agent treatment of stroke treatment of neurodegeneration
AUTHOR(S): Sorbera, L. A.; Castaner, J.; Castaner, R. M.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2004), 29(5), 441-448
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

TI Arundic Acid: Astrocyte-modulating agent treatment of stroke treatment of neurodegeneration

AB A review. According to the World Health Organization, stroke is the leading cause of death worldwide, accounting for 5 million deaths per yr. Oxygen deprivation due to stroke leads to rapid nerve cell death and dysfunction of the body part controlled by the affected nerve cells. Thus, stroke is also responsible for serious long-term disability (e.g., paralysis, cognitive deficits, dementia, dizziness, vertigo, impaired vision, language deficits, emotional difficulties, pain). Although there have been improvements in recent years in the treatment of stroke, the need for novel therapies to prevent and treat stroke remains a research priority. One novel agent to emerge is Ono-2506 (arundic acid), which modulates astrocyte activation by inhibiting the enhanced astrocytic synthesis of S-100β, responsible for inducing neuronal death. Ono-2506 does not affect thrombi or blood vessels and therefor does not pose a risk for hemorrhage. It has shown efficacy in preventing expansion of cerebral infarction by improving astrocyte function and may be effective even when administered hours after ischemic stroke onset. Ono-2506 is undergoing phase II development for the treatment of acute ischemic stroke, as well as clin. development in other neurodegenerative diseases including amytrophic lateral sclerosis, Alzheimer's disease and Parkinson's disease.

ST review arundic acid neurodegenerative disease ischemia brain stroke astrocyte

IT Hemorrhage
(Onol-2506 does not affect thrombi or blood vessels and therefor does not pose risk for hemorrhage and is in phase II trial to treat acute ischemic stroke and other neurodegenerative disease in humans)

IT Alzheimer's disease
(Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat Alzheimer's disease in patient)

IT Parkinson's disease
(Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat Parkinson's disease in patient)

IT Human
(Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat neurodegenerative disease in humans)

IT Astrocyte
Brain
(Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat neurodegenerative disease in patient)

IT Nervous system, disease
(amyotrophic lateral sclerosis; Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat amyotrophic lateral sclerosis patient)

IT Nervous system, disease
(degeneration; Onol-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset

and is in phase II trial to treat neurodegenerative disease in patient)

IT Brain, disease
(stroke; Ono1-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat neurodegenerative disease in patient)

IT 185517-21-9P, Ono-2506
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Ono1-2506 is effective in preventing cerebral infarction expansion by improving astrocyte function, may be effective when administered hours after ischemic stroke onset and is in phase II trial to treat neurodegenerative disease in patient)

L4 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2004:407030 CAPLUS
DOCUMENT NUMBER:	141:1101
TITLE:	Attenuation of a delayed increase in the extracellular glutamate level in the peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506
AUTHOR(S):	Mori, Takashi; Tateishi, Narito; Kagamiishi, Yoshifumi; Shimoda, Taiji; Satoh, Souichi; Ono, Sakiko; Katsube, Nobuo; Asano, Takao
CORPORATE SOURCE:	Institute of Laboratory Animal Science, Saitama Medical Center/School, Kawagoe, Saitama, 350-8550, Japan
SOURCE:	Neurochemistry International (2004), 45(2-3), 381-387 CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OS.CITING REF COUNT:	13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT:	30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Attenuation of a delayed increase in the extracellular glutamate level in the peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506

AB A novel agent, ONO-2506 [(R)-(-)-2-propyloctanoic acid, ONO Pharmaceutical Co. Ltd.] was previously shown to mitigate delayed infarct expansion through inhibition of the enhanced production of S-100β, while inducing a prompt symptomatic improvement that attained a significant level as early as 24 h after drug administration. To elucidate the mechanism underlying the prompt symptomatic improvement, the present study aimed to examine whether ONO-2506 modulates the level of extracellular glutamate ([Glu]e) in the rat subjected to transient middle cerebral artery occlusion (tMCAO). In this model, it had been shown that ONO-2506 reduces the infarct volume, improves the neurol. deficits, and enhances the mRNA expression of glial glutamate transporters (GLT-1 and GLAST). The [Glu]e levels in the ischemic cortices were continuously measured using intracerebral microdialysis. The alterations in the [Glu]e levels in the sham-operated and tMCAO-operated groups with or without drug administration were compared. In the tMCAO groups, the [Glu]e level increased during tMCAO to a similar extent, returned to normal on reperfusion, and increased again around 5 h. In the saline-treated group, however, the [Glu]e level further increased from 15 h on to reach about 280% of the normal level at 24 h. This secondary increase in the [Glu]e level in the late phase of reperfusion was prevented by ONO-2506. The intracerebral infusion of glutamate transporter inhibitor,

1-trans-pyrrolidine-2,4-dicarboxylic acid, at 24 h after tMCAO induced an increase in the [Glu]e level, which was marked in both the sham-operated and ONO-2506-treated groups, but much less pronounced in the saline-treated group. The above results suggest that functional modulation of activated astrocytes by pharmacol. agents like ONO-2506 may inhibit the secondary rise of [Glu]e level in the late phase of reperfusion, leading to amelioration of delayed infarct expansion and neurol. deficits.

ST ONO 2506 focal cerebral ischemia treatment extracellular glutamate; brain infarction treatment ONO 2506 extracellular glutamate

IT Neuroglia
(attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Ischemia
(cerebral focal; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glutamate transporter SLC1A2; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glutamate transporter, GLAST; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Brain, disease
(infarction; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Brain, disease
(ischemia, focal; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT 56-86-0, L-Glutamic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

IT 185517-21-9, ONO-2506
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuation of a delayed increase in extracellular glutamate level in peri-infarct area following focal cerebral ischemia by a novel agent ONO-2506 in relation to role or glial glutamate transporters)

L4 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:739273 CAPLUS
DOCUMENT NUMBER: 140:122721
TITLE: Functional modulation of astrocytes by a novel agent ONO-2506 mitigates delayed infarct expansion with a wide therapeutic time window, inducing prompt neurological recovery through reduction of the extracellular level of glutamate
AUTHOR(S): Asano, Takao; Tateishi, Narito N.; Matsui, Tohru; Mori, Takashi; Kagamiishi, Yoshifumi; Sato, Souichi; Katsube, Nobuo
CORPORATE SOURCE: Department of Neurosurgery, Saitama Medical Center/School, Saitama, 350-8550, Japan
SOURCE: International Congress Series (2003), 1252(Molecular Mechanism and Epochal Therapeutics of Ischemic Stroke and Dementia), 147-151
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Ischemia
(transient focal cerebral; effect of ONO-2506 on astrocytes and extracellular glutamate in focal ischemia)
IT 185517-21-9, ONO-2506
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of ONO-2506 on astrocytes and extracellular glutamate in focal ischemia)

L4 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:700823 CAPLUS
DOCUMENT NUMBER: 139:270134
TITLE: ONO-2506(Ono)
AUTHOR(S): de Paulis, Tomas
CORPORATE SOURCE: Psychiatry Department, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(7), 863-867
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. ONO-2506 is an enantiomeric, three carbon atom homolog of valproic acid under development by ONO Pharmaceutical for the potential treatment of stroke, as well as Alzheimer's and Parkinson's diseases. The injectable formulation (Proglia) is undergoing phase II trials in the US and Japan for acute-phase cerebral infarction, and the oral formulation (Cereact) is in phase I trials in the UK for Alzheimer's disease (AD) and Parkinson's disease (PD). Japanese and European phase I trials for AD, PD and amyotrophic lateral sclerosis (ALS) had commenced by Mar. 2002 and phase II trials for ALS are underway in Europe.
ST review neuroprotectant ONO2506 Parkinson Alzheimer disease ALS stroke
IT Alzheimer's disease

Anti-Alzheimer's agents
Anti-inflammatory agents
Antiparkinsonian agents
Human
Parkinson's disease
(ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Nervous system, disease
(amyotrophic lateral sclerosis; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Ischemia
(cerebral; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Brain, disease
(infarction; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Brain, disease
(ischemia; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Cytoprotective agents
Nervous system agents
(neuroprotective agents; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT Brain, disease
(stroke; ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

IT 185517-21-9P, ONO 2506
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ONO-2506 for treatment of patients with Alzheimer's disease, cerebral infarction, cerebrovascular ischemia, motor neuron disease, neurol. disease, and Parkinson's disease)

L4 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:110346 CAPLUS
DOCUMENT NUMBER: 138:289331
TITLE: Process Development of ONO-2506: A Therapeutic Agent for Stroke and Alzheimer's Disease
AUTHOR(S): Hasegawa, Tomoyuki; Kawanaka, Yasufumi; Kasamatsu, Eiji; Iguchi, Yoichi; Yonekawa, Yoshihira; Okamoto, Masaki; Ohta, Chiaki; Hashimoto, Shinsuke; Ohuchida, Shuichi
CORPORATE SOURCE: Chemical Process Research Laboratories, Fukui Research Institute, Ono Pharmaceutical Co. Ltd., Yamagishi, Mikuni, Sakai, Fukui, 913-8538, Japan
SOURCE: Organic Process Research & Development (2003), 7(2), 168-171
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:289331
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Process Development of ONO-2506: A Therapeutic Agent for Stroke and Alzheimer's Disease
IT Chiral auxiliary
Recrystallization
(in process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT Alzheimer's disease
Drugs
(process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT Chemical engineering design
(scale-up; process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT Allylation
(stereoselective; in process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT Brain, disease
(stroke; process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT 141341-55-1P 213914-68-2P 213914-70-6P 287731-56-0P 506436-72-2P 506436-73-3P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(in process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT 106-95-6, Allyl bromide, reactions 111-64-8, Octanoyl chloride 7757-83-7, Sodium sulfite 94594-90-8, (1S)-(-)-10,2-Camphorsultam
RL: RCT (Reactant); RACT (Reactant or reagent)
(in process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)
IT 185517-21-9P
RL: IMF (Industrial manufacture); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process development of ONO-2506: a therapeutic agent for stroke and Alzheimer's disease)

L4 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:76651 CAPLUS
DOCUMENT NUMBER: 138:131143
TITLE: Remedies for brain ischemic diseases
INVENTOR(S): Honjo, Kaneyoshi; Tateishi, Narito; Katsube, Nobuo
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007992	A1	20030130	WO 2002-JP7212	20020716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

CA 2453478	A1	20030130	CA 2002-2453478		20020716
AU 2002318567	A1	20030303	AU 2002-318567		20020716
EP 1415668	A1	20040506	EP 2002-746090		20020716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 4178405	B2	20081112	JP 2003-513597		20020716
EP 2050468	A1	20090422	EP 2009-152065		20020716
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR, AL, LT, LV, MK, RO, SI					
US 20040176347	A1	20040909	US 2004-483629		20040114
US 20070219177	A1	20070920	US 2007-753425		20070524
KR 2008100290	A	20081114	KR 2008-726004		20081023
PRIORITY APPLN. INFO.:			JP 2001-217755	A	20010718
			EP 2002-746090	A3	20020716
			WO 2002-JP7212	W	20020716
			US 2004-483629	A3	20040114
			KR 2004-700620	A3	20040115

OTHER SOURCE(S): MARPAT 138:131143
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Hemorrhage
Ischemia
(cerebral; neuroprotectants and thrombolytics as remedies for brain ischemic diseases)
IT Brain, disease
(infarction; neuroprotectants and thrombolytics as remedies for brain ischemic diseases)
IT 139639-23-9, Tissue plasminogen activator 185517-21-9
185517-21-9D, salts and hydrates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotectants and thrombolytics as remedies for brain ischemic diseases)

L4 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:520052 CAPLUS
DOCUMENT NUMBER: 138:66447
TITLE: Astrocytic activation and delayed infarct expansion after permanent focal ischemia in rats. Part II: Suppression of astrocytic activation by a novel agent (R)-(-)-2-propyloctanoic acid (ONO-2506) leads to mitigation of delayed infarct expansion and early improvement of neurologic deficits
AUTHOR(S): Tateishi, Narito; Mori, Takashi; Kagamiishi, Yoshifumi; Satoh, Souichi; Katsube, Nobuo; Morikawa, Eiharu; Morimoto, Tadashi; Matsui, Toru; Asano, Takao
CORPORATE SOURCE: Minase Research Institute, Ono Pharmaceutical Co. Ltd., Osaka, Japan
SOURCE: Journal of Cerebral Blood Flow and Metabolism (2002), 22(6), 723-734
CODEN: JCBMDN; ISSN: 0271-678X
PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English
OS.CITING REF COUNT: 53 THERE ARE 53 CAPLUS RECORDS THAT CITE THIS RECORD (53 CITINGS)
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A novel agent, (R)-(-)-2-propyloctanoic acid (ONO-2506), has a unique property in that it modulates functions of activated cultured astrocytes, including pronounced inhibition of S-100β synthesis. The present study examined whether administration of this agent would mitigate the delayed expansion of infarct volume and the neurol. deficits after permanent middle cerebral artery occlusion (pMCAO) in rats. Daily i.v. administration of ONO 2506 (10 mg/kg) abolished the delayed infarct expansion between 24 and 168 h after pMCAO, whereas the acute infarct expansion until 24 h was unaffected. The agent significantly reduced the expression of S-100β and glial fibrillary acidic protein in the activated astrocytes and the number of terminal deoxynucleotidyl transferase-mediated 2'-deoxyuridine 5'-triphosphatebiotin nick end labeling-pos. cells in the periinfarct area. The neurol. deficits were significantly improved, compared with the vehicle-treated groups, as early as 24 h after the initial administration of ONO-2506. The agent had a wide therapeutic time window of 0 to 48 h after pMCAO. These results indicate that because of the pharmacol. modulation of astrocytic activation induced by ONO 2506, symptoms can regress whereas delayed expansion of the lesion is arrested. Pharmacol. modulation of astrocytic activation may confer a novel therapeutic strategy against stroke
.

ST ONO 2506 astrocytic activation brain infarction focal ischemia

IT Ischemia
(cerebral focal; suppression of astrocytic activation by ONO 2506 leads to mitigation of delayed infarct expansion and early improvement of neurol. deficits)

IT Brain, disease
(infarction; suppression of astrocytic activation by ONO 2506 leads to mitigation of delayed infarct expansion and early improvement of neurol. deficits)

IT Brain, disease
(stroke; suppression of astrocytic activation by ONO 2506 leads to mitigation of delayed infarct expansion and early improvement of neurol. deficits)

IT 185517-21-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression of astrocytic activation by ONO 2506 leads to mitigation of delayed infarct expansion and early improvement of neurol. deficits)

L4 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:372897 CAPLUS
DOCUMENT NUMBER: 122:160096
ORIGINAL REFERENCE NO.: 122:29501a,29504a
TITLE: Preparation of valproate analogs as neuroprotectants
INVENTOR(S): Ohuchida, Shuichi; Kishimoto, Kazuo; Tateishi, Narito; Ohno, Hiroyuki
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 632008	A1	19950104	EP 1994-108330	19940530
EP 632008	B1	19980204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 163006	T	19980215	AT 1994-108330	19940530
ES 2113574	T3	19980501	ES 1994-108330	19940530
CA 2124784	A1	19941202	CA 1994-2124784	19940531
CA 2124784	C	20030107		
JP 07316092	A	19951205	JP 1994-140957	19940531
JP 2756756	B2	19980525		
CN 1100408	A	19950322	CN 1994-106203	19940601
CN 1083419	C	20020424		
KR 225299	B1	19991015	KR 1994-12261	19940601
US 6201021	B1	20010313	US 1996-681482	19960723
JP 09118644	A	19970506	JP 1996-216932	19960731
JP 10204023	A	19980804	JP 1998-32255	19980129
JP 2935110	B2	19990816		
JP 10324626	A	19981208	JP 1998-155577	19980604
JP 3195581	B2	20010806		
CN 1322524	A	20011121	CN 2000-127088	20000908
CN 1200703	C	20050511		
US 20030096802	A1	20030522	US 2002-194247	20020715
US 7176240	B2	20070213		
US 20050261371	A1	20051124	US 2005-192004	20050729
US 7569609	B2	20090804		
US 20050261167	A1	20051201	US 2005-192002	20050729
US 7569608	B2	20090804		
US 20050261168	A1	20051201	US 2005-192003	20050729

PRIORITY APPLN. INFO.:

JP 1993-154331	A	19930601
JP 1993-301067	A	19931105
JP 1994-80982	A	19940328
JP 1994-140957	A3	19940531
JP 1996-216932	A3	19940531
US 1994-252642	B1	19940601
US 1996-681482	A3	19960723
US 2000-661054	B1	20000913
US 2002-194247	A1	20020715

OTHER SOURCE(S): MARPAT 122:160096

OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (84 CITINGS)

IT Brain, disease
(stroke, treatment; preparation of valproate analogs as neuroprotectants)

IT 99-66-1P 149-57-5P 1575-72-0P 3274-28-0P 5558-45-2P 5732-83-2P
13949-65-0P 15331-26-7P 19986-16-4P 20406-74-0P 22635-29-6P
28396-40-9P 31080-39-4P 31080-41-8P 33786-47-9P
35841-43-1P 50632-58-1P 51679-74-4P 60948-96-1P 65185-82-2P
78435-49-1P 88223-42-1P 93273-42-8P 98191-23-2P 120254-13-9P
143100-15-6P 158017-53-9P 158017-54-0P 161088-98-8P 161088-99-9P
161089-00-5P 161089-01-6P 161089-02-7P 161089-03-8P 161089-04-9P
161089-05-0P 161089-06-1P 161089-07-2P 161089-08-3P 161089-09-4P
161089-10-7P 161089-11-8P 161089-12-9P 161089-13-0P 161089-14-1P
161089-15-2P 161089-16-3P 161089-17-4P 161089-19-6P 161089-20-9P
161089-21-0P 161089-22-1P 161089-23-2P 161089-24-3P 161089-25-4P
161089-26-5P 161089-27-6P 161089-28-7P 161089-29-8P 161089-30-1P
161089-31-2P 161089-32-3P 161089-33-4P 161089-34-5P 161089-35-6P
161089-36-7P 161089-37-8P 161089-38-9P 161089-39-0P 161089-40-3P
161089-41-4P 161089-42-5P 161089-43-6P 161089-44-7P 161089-45-8P
161089-46-9P 161089-47-0P 161089-48-1P 161089-49-2P 161089-51-6P
161089-52-7P 161089-53-8P 161089-54-9P 161089-55-0P
161089-56-1P 161089-57-2P 161089-58-3P 161089-59-4P 161089-60-7P
161089-61-8P 161089-62-9P 161089-63-0P 161089-64-1P 161089-65-2P

161089-66-3P 161089-67-4P 161089-68-5P 161089-69-6P 161089-70-9P
161089-71-0P 161089-72-1P 161089-73-2P 161089-74-3P 161089-75-4P
161089-76-5P 161089-77-6P 161089-78-7P 161089-84-5P 161089-85-6P
161089-86-7P 161089-87-8P 161089-88-9P 161089-89-0P 161089-90-3P
161089-92-5P 161089-93-6P 161089-94-7P 161089-97-0P 161089-99-2P
161090-00-2P 161090-01-3P 161090-04-6P 161090-12-6P 161090-13-7P
161090-14-8P 161090-15-9P 161090-16-0P 161090-17-1P 161169-28-4P
161169-29-5P 178269-53-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of valproate analogs as neuroprotectants)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	114.36	300.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-18.86	-18.86

STN INTERNATIONAL LOGOFF AT 14:11:29 ON 29 SEP 2009